

Chemoprevention

Chemoprevention is the use of natural or synthetic substances to reduce the risk of developing cancer, or to reduce the chance that cancer will recur (come back). The National Cancer Institute's (NCI) chemoprevention research effort started in the early 1980s and has grown considerably since that time. Currently, approximately 400 compounds are being studied as potential chemopreventive agents, mainly in laboratory research. Over 40 of these compounds are being studied in clinical trials (research studies with people). Some of these agents are being investigated as single agents; others are being tested in combinations of two drugs. Chemoprevention trials look at possible ways to prevent cancer with interventions that include drugs, vitamins, diet, hormone therapy, or other agents.

To identify possible chemopreventive agents, scientists analyze data obtained from studies of selected groups of people. For example, scientists might study a group with a lower-than-average rate of cancer to determine what factors could be protecting them from the disease. They might find that people who eat certain foods develop cancer less often than those who do not. The scientists might then isolate compounds from these foods and test their ability to prevent, halt, or reverse cancer development in cells grown in the laboratory. Compounds showing promise in these tests may be examined further in animals. When a substance shows promise in such studies, researchers may then evaluate it in clinical trials. For example, a clinical trial is being conducted to investigate the effectiveness of budesonide (an asthma drug)



in preventing lung cancer. Scientists also test chemopreventive substances in people at high risk for cancer because of a precancerous condition, a family history of cancer, lifestyle factors such as smoking, or other factors. Other research involves people who have had cancer and have an increased chance of recurrence. More information is available on the NCI's Chemopreventive Agent Development Research Group's Web site at <http://www3.cancer.gov/prevention/cadrg> on the Internet.

Five classes of chemopreventive agents have shown promise in clinical trials and are considered priority substances for study. These agents include selective estrogen receptor modulators (SERMS) such as tamoxifen, and other hormonal agents; nonsteroidal anti-inflammatory drugs (NSAIDS); calcium compounds; glucocorticoids (compounds that are a type of steroid); and retinoids (chemical cousins of vitamin A).

Data reported in 1998 from the Breast Cancer Prevention Trial (BCPT) showed that women taking tamoxifen had 49 percent fewer diagnosed cases of breast cancer. These results were the first clear indication that a chemopreventive agent could be effective in preventing cancer in a high-risk population. But because tamoxifen was associated with serious side effects, such as endometrial cancer and blood clots, researchers are comparing raloxifene (another SERM) with tamoxifen in the Study of Tamoxifen and Raloxifene (STAR) trial.

The NCI is currently sponsoring the Prostate Cancer Prevention Trial (PCPT) to see if the drug finasteride (used to treat patients with symptomatic noncancerous enlargement of the prostate, also called benign prostatic hyperplasia) can prevent prostate cancer in men who are age 55 or older. Finasteride reduces levels of dihydrotestosterone (DHT), a male hormone that is important in normal and abnormal prostate growth.

NSAIDS, such as aspirin, piroxicam, celecoxib, and sulindac, are being studied alone and in combination with other agents to see if they are useful preventive agents for people with a family history of colon polyps or cancer. In 1999, the Food and Drug Administration (FDA) approved the use of celecoxib to reduce the number of colorectal polyps in people with familial adenomatous polyposis (FAP), an inherited condition in which hundreds of polyps form in the colon and rectum. It is not yet known whether using celecoxib to reduce the number of polyps will also reduce the number of new cases or deaths from colorectal cancer. The NCI is also sponsoring chemoprevention trials studying the use of celecoxib for people at risk of cancers of the esophagus and bladder.

Calcium compounds are being studied for the prevention of colon cancer. These studies are being conducted mainly in people previously diagnosed with colon polyps or cancer.

Budesonide, a glucocorticoid used to treat asthma, is being studied in clinical trials to prevent the progression of precancerous changes in lung tissue. The drug is being given as a spray so that it reaches the lung tissue directly.

Scientists are also studying synthetic and natural retinoids alone and with other compounds for the prevention of several types of cancer, including cancers of the cervix, lung, oral cavity, and bladder. Other agents currently being investigated are selenium, vitamin E, 2-difluoromethylornithine (DFMO) (also called eflornithine), folic acid, oltipraz, and genistein.

NCI Priorities for Chemoprevention Research

In July 1998, NCI's Division of Cancer Prevention (DCP) convened the Chemoprevention Implementation Group (CIG) to further define and guide research in the field of chemopreventive agents. Members of the CIG included NCI staff and researchers outside the

NCI, who represent a variety of disciplines related to chemoprevention. The CIG's task was to

- 1) set priorities for agents to be developed and evaluated in chemoprevention clinical trials;
- 2) provide advice on the best designs for chemoprevention clinical studies; 3) identify research challenges and opportunities for chemoprevention; and 4) develop strategies for advancing chemoprevention research, such as attracting new scientists to the field. For a copy of the CIG's report, contact the Cancer Information Service (CIS) at 1-800-4-CANCER (1-800-422-6237) or visit the NCI's Publications Locator Web site at <http://cancer.gov/publications> on the Internet.

The DCP's Rapid Access to Preventive Intervention Development (RAPID) program was initiated as a result of recommendations made by the CIG. RAPID is designed to make NCI resources available to the research community for the preclinical and early clinical development of potential chemopreventive agents. The goal of RAPID is to facilitate the process of bringing discoveries from the laboratory to clinical trials.

Additional initiatives are planned for the development of animal models, the discovery of potential chemopreventive agents using technology from cancer genetics research, and the scientific validation of measures used to evaluate the effectiveness of chemopreventive agents.

The Future of Chemoprevention Research

Although scientists have some evidence that certain compounds may help prevent cancer in populations at higher risk, only large clinical trials conducted for many years with thousands of people can demonstrate whether a compound will reduce the risk of cancer in the general population. For more information about ongoing chemoprevention clinical trials, contact the CIS at the telephone number listed below or visit the clinical trials page of the NCI's Web site at http://cancer.gov/clinical_trials/ on the Internet.

#

Sources of National Cancer Institute Information

Cancer Information Service

Toll-free: 1-800-4-CANCER (1-800-422-6237)

TTY (for deaf and hard of hearing callers): 1-800-332-8615

NCI Online

Internet

Use <http://cancer.gov> to reach the NCI's Web site.

LiveHelp

Cancer Information Specialists offer online assistance through the *LiveHelp* link on the NCI's Web site.

This fact sheet was reviewed on 5/13/02